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**Crystal Structure of The Ternary Complex of *E. coli* ADP-ribose pyrophosphatase, an ADP-ribose Analog and Magnesium: A Step Towards Its Mechanism.**

S.B. Gabelli, M.A. Bianchet, Y. Ohnishi, Y. Ichikawa, M.J. Bessman, L.M. Amzel (Johns Hopkins University)

Beamline(s): X25

**Introduction:** *E. coli* ADPR-ase, a housecleaning Nudix enzyme, catalyses the hydrolysis of ADP-ribose to AMP and ribose-5-P.

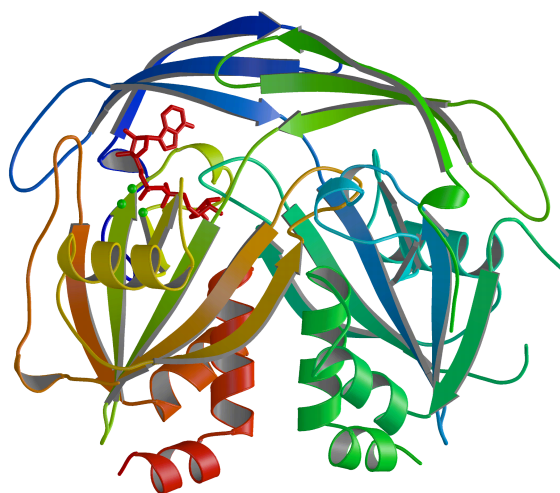
**Methods and Materials:** The ternary complex of ADPR-ase <sup>[1]</sup> with the non hydrolyzable  $\alpha,\beta$ -methylene ADP-ribose analog, AMPCPR, and  $Mg^{+2}$  was determined with data to 2.0Å resolution collected on a CCD detector (Brandeis B4) at Beamline X25 at NSLS, Brookhaven National Laboratory. Diffraction data, processed with Denzo and Scalepack, have an  $R_{sym}$  of 11%. The model was refined using the CNS suite with a residual target to  $R_{crys}=19\%$  ( $R_{free}=24\%$ ).

**Results:** The structure of the ternary complex of ADPR-ase with the non hydrolysable AMPCPR and  $Mg^{+2}$  shows that the attacking water molecule is activated by bridging two Magnesium atoms with a glutamate functioning as the catalytic base. The oxygen of the attacking water is in molecular contact (3.0Å) with the phosphorous of the adenosyl phosphate forming an angle of 177° with the scicile bond. These observations suggest that the reaction occurs via an associative mechanism.

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**References:**

[1]. S.B. Gabelli, M.A. Bianchet, M.J. Bessman and L.M. Amzel. The structure of ADP-ribose pyrophosphatase reveals the structural basis for the versatility of the Nudix family. *Nature Structural Biology*, 8 (5) 467-472



Structure of the ADPRase in complex with AMPCPR